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NEWS EXPRESS FEBRUARY 08 CURRENT WINDOWS VERSION IS V8.3, AND CURRENT DISCOVER FILE IS DATED 20 FEBRUARY 2008

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FILE 'MEDLINE' ENTERED AT 09:47:23 ON 25 MAR 2008

-> s rotaxane (1) (complex or inclusion or host)

L1 898 ROTAXANE (L) (COMPLEX OR INCLUSION OR HOST)

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ENTER L# LIST OR (END):11

PROCESSING COMPLETED FOR L1 L2 730 DUP REM L1 (168 DUPLICATES REMOVED)

=> s 12 and py<=2003

.3 430 L2 AND PY<=2003

=> s 13 and rotaxane (s) (complex or inclusion or host)
L4 331 L3 AND ROTAXANE (S) (COMPLEX OR INCLUSION OR HOST)

=> d scan 14

L4 331 ANSWERS CAPLUS COPYRIGHT 2008 ACS on STN

22-3 (Physical Organic Chemistry) Section cross-reference(s): 75

TI First Pseudorotaxane-Like [3]Complexes Based on Cryptands and Paraquat: Self-Assembly and Crystal Structures

ST pseudorotaxane inclusion complex cryptand paraquat base prepn crystallog

IT Formation constant

(association constant; preparation and crystallog. of pseudorotaxane-like complexes based on cryptands and paraguat)

IT Crystal structure

Encapsulation Hydrogen bond

Molecular structure

Self-assembly

(preparation and crystallog. of pseudorotaxane-like complexes based on cryptands and paraquat)

IT Cryptands

RL: CPS (Chemical process); PEP (Physical, engineering or chemical

process); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)

(preparation and crystallog. of pseudorotaxane-like complexes based on cryptands and paraguat)

T Inclusion compounds

RL: FMU (Formation, unclassified); PRP (Properties); FORM (Formation, nonpreparative)

(preparation and crystallog. of pseudorotaxane-like complexes based on cryptands and paraguat)

IT NMR (nuclear magnetic resonance)

(proton; preparation and crystallog. of pseudorotaxane-like complexes based on cryptands and paraquat)

IT Rotaxanes

RL: FMU (Formation, unclassified); PRP (Properties); FORM (Formation, nonpreparative)

(pseudorotaxanes; preparation and crystallog. of pseudorotaxane-like complexes based on cryptands and paraquat)

IT 591767-50-9P 591767-51-0P

RL: PRP (Properties); SPM (Synthetic preparation); PREP (Preparation) (crystal structure; preparation and crystallog, of pseudorotaxane-like complexes based on cryptands and paraquat)

IT 64739-07-7 106376-99-2

RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); PRP (Properties); RCT (Reactant); PROC (Process); RACT (Reactant or reagent)

(preparation and crystallog. of pseudorotaxane-like complexes based on cryptands and paraquat)

T 249925-32-4

RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); RCT (Reactant); PROC (Process); RACT (Reactant or reagent) (preparation and crystallog. of pseudorotaxane-like complexes based on cryptands and paraquat)

T 591767-47-4P

RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); PROC (Process); RACT (Reactant or reagent) (preparation and crystallog. of pseudorotaxane-like complexes based on

cryptands and paraquat)

II 591767-49-6
RL: FMU (Formation, unclassified); RCT (Reactant); FORM (Formation, nonpreparative); RACT (Reactant or reagent)

(preparation and crystallog. of pseudorotaxane-like complexes based on cryptands and paraquat)

IT 108-73-6, Phloroglucinol 4685-14-7, Paraquat RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation and crystallog. of pseudorotaxane-like complexes based on cryptands and paraguat)

IT 59291-87-1P, 5-Benzyloxyresorcinol 591767-46-3P 591767-48-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(preparation and crystallog. of pseudorotaxane-like complexes based on cryptands and paraguat)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

=> end

ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF LOGOFF? (Y)/N/HOLD:n

=> s rotaxane and (drug (s) delivery)

1 FILES SEARCHED...

75 ROTAXANE AND (DRUG (S) DELIVERY)

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=> s 15 and py<=2003
L6 37 L5 AND PY<=2003
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=> dup rem ENTER L# LIST OR (END):16 PROCESSING COMPLETED FOR L6

35 DUP REM L6 (2 DUPLICATES REMOVED)

=> d 17 ibib abs 1-35

L7 ANSWER 1 OF 35 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:681395 CAPLUS

DOCUMENT NUMBER: 2004:881393 C

TITLE: Multivalently interactive molecular assembly, capturing agent, drug carrier, calcium chelating

agent, and drug enhancer

INVENTOR(S): Yui, Nobuhiko; Maruyama, Atsushi; Ooya, Tooru

PATENT ASSIGNEE(S): Japan

SOURCE: U.S. Pat. Appl. Publ., 47 pp., Cont.-in-part of U.S.

Pat. Appl. 2003 171,573. CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004162275	A1	20040819	US 2003-679499	20031007
US 2003171573	A1	20030911	US 2002-230394	20020829 <
PRIORITY APPLN. INFO.:			JP 2002-52474 A	20020227
			US 2002-230394 B2	20020829

AB A multivalently interactive mol. assembly having a plurality of functional groups or ligands, in which a ratio between Rh and Rg expressed as Rh/Rg is 1.0 or less. Here, Rh is a hydrodynamic radius calculated from dynamic light scattering (DLS) assay performed in aqueous solution; and Rg is a radius of

gyration determined based on the Zimm plot generated using data obtained by static light scattering (SLS) assay. A polyrotaxane was prepared from α -cyclocaxtrin and diamino-PEG and reacted with Z-L-Phe succinimide ester. Then biotin mols. were introduced into the polyrotaxane mol. Examples were given of anal. of biotin-polyrotaxane conjugate binding to streptavidin-immobilized surface using surface plasmon resonance. Trypsin activity inhibition and Ca chelating activities of polyrotaxanes were also given.

L7 ANSWER 2 OF 35 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:5802 CAPLUS

DOCUMENT NUMBER: 138:66692

TITLE: Tissue-specific transporter inhibitor in treatment of tissue dysfunction diseases and chronic renal failure INVENTOR(S): Tsuji, Akira; Tamai, Ikumi; Sai, Yoshimichi; Yul

Noubuhiko; Oya, Toru; Miyamoto, Ken-ichi

PATENT ASSIGNEE(S): Japan Science and Technology Corporation, Japan

SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PAT	PATENT NO.				KIND DATE		APPLICATION NO.					DATE						
WO	2003				A1	-	2003	0103	WC	20	002-	JP61	04			0020		<
				CH,	CY,	DE,	DK,	ES,	FI, F	R,	GB,	GR,	IE,	IT,	LU,	MC,	NL,	
JP	2003	0028	43		A		2003	0108	JP	20	001-	1888	43		2	0010	621	<
JP	3942	846			B2		2007	0711										
CA	2451	433			A1		2003	0103	CA	. 20	002-	2451	433		2	0020	619	<
CA	2451	433			C		2007	1030										
AU	2002	3132	42		A1		2003	80108	AU	20	002-	3132	42		2	0020	619	<
EP	1405	644			A1		2004	10407	EP	20	002-	7387	67		2	0020	619	
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB, G	R,	IT,	LI,	LU,	NL,	SE,	MC,	PT,	
		IE,	FI,	CY,	TR													
US	2004	1912	11		A1		2004	10930	US	20	003-	7423	35		2	0031	219	
PRIORITY	APP	LN.	INFO	. :					JP	20	001-	1888	43	- 1	A 2	0010	621	
									WC	20	002-	JP61	04	1	ii 2	0020	619	

AB It is intended to provide a tissue-specific transporter inhibitor which is not absorbed in the digestive tract and can prevent worsening in the quality of life (QCL) of a patient due to diet therapy; and remedies for tissue dysfunction diseases and remedies for chronic renal failure progress containing the above inhibitor as the active ingredient. The tissue-specific transporter inhibitor not absorbed in the digestive tract is prepared by introducing a dipeptide which is a ligand of oligopeptide transporter I into a supermol. structure polyrotaxane which is expected as being excellent in the interaction of its structurally modified active residue with a transmembrane transporter.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 35 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:717792 CAPLUS

DOCUMENT NUMBER: 139:224476

TITLE: Multivalently interactive molecular assembly, capturing agent, drug carrier, calcium chelating

agent, and drug enhancer

INVENTOR(S): Yui, Nobuhiko; Maruyama, Atsushi; Ooya, Tooru

PATENT ASSIGNEE(S): Japan SOURCE: U.S. P

SOURCE: U.S. Pat. Appl. Publ., 33 pp. CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
				-		
US 2003171573	A1	20030911	US 2002-230394		20020829	<
JP 2004027183	A	20040129	JP 2003-51163		20030227	
US 2004162275	A1	20040819	US 2003-679499		20031007	
PRIORITY APPLN. INFO.:			JP 2002-52474	A	20020227	
			US 2002-230394	Α	20020829	

AB The invention relates to a multivalently interactive mol. assembly which can effectively and stably bind to a target substance in vivo or in vitro, a capturing agent comprising said multivalently interactive mol. assembly for capturing an object of interest in vivo or in vitro, a drug carrier which aids administration of a drug, a calcium chelating agent which can effectively chelate calcium, and a drug enhancer which can be administered with a drug to assist in e.g. absorption of the drug. The invention discloses a multivalently interactive mol. assembly having a plurality of functional groups or ligands, in which a ratio between Rh and Rg expressed as Rn/Rg is 1.0 or less. Here, Rh is a hydrodynamic radius calculated from a

dynamic light scattering assay performed in aqueous solution, and $\ensuremath{\mathsf{Rg}}$ is a radius

of gyration determined based on the Zimm plot generated using data obtained by a static light scattering assay. Specifically, the invention discloses polyrotaxanes, the synthesis of which is described.

L7 ANSWER 4 OF 35 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:558225 CAPLUS

DOCUMENT NUMBER: 140:117028

TITLE: Polyrotaxanes: challenge to multivalent binding with

biological receptors on cell surfaces

AUTHOR(S): Yui, Nobuhiko; Ooya, Tooru

CORPORATE SOURCE: Japan Advanced Institute of Science and Technology,

Tatsunokuchi, Ishikawa, 923-1292, Japan SOURCE: Materials Science Forum (2003), 426-432(Pt.

SOURCE: Materials Science Forum (2003), 426-432(Pt. 4, THERMEC'2003), 3243-3248

CODEN: MSFOEP; ISSN: 0255-5476

PUBLISHER: Trans Tech Publications Ltd.
DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. The challenge to multivalent binding between ligands and proteins or biol. receptors on cell surfaces has been focused on using supramol.-structured polymers, polyrotaxanes. Our designed polyrotaxanes

consist of ligand-immobilized α -cyclodextrins (α -CDs) threaded onto a linear polymeric chain (polyethylene glycol) (PEG) capped both terminals with bulky end-groups via biodegradable linkages. Structural characteristics of these polyrotaxanes involve sliding and rotational motion of the ligands immobilized on α -CDs along a PEG chain as to

easily face to binding sites on proteins, which can contribute much to enhanced multivalent binding with proteins.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 35 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:489737 CAPLUS DOCUMENT NUMBER: 140:47100

TITLE: Approach to multivalent biological interactions by

using supermolecular biomaterials

AUTHOR(S): Yui, Nobuhiko

CORPORATE SOURCE: Japan Advanced Institute of Science and Technology,

Japan

SOURCE: Gekkan Yakuji (2003), 45(7), 1269-1272

CODEN: YAKUD5; ISSN: 0016-5980

PUBLISHER: Jiho

DOCUMENT TYPE: Journal; General Review

LANGUAGE: Japanese

AB A review especially covering multivalent interaction of ligand-introduced α-cvclodextrin/polyethylene glycol-based polyrotaxanes with proteins

for their application as biomaterials.

7 ANSWER 6 OF 35 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:819708 CAPLUS

DOCUMENT NUMBER: 140:391507

TITLE: Rotaxane dendrimers

AUTHOR(S): Lee, Jae Wook; Kim, Kimoon

CORPORATE SOURCE: Department of Chemistry, Dong-A University, Pusan,

604-714, S. Korea

SOURCE: Topics in Current Chemistry (2003),

228(Dendrimers V), 111-140

CODEN: TPCCAQ; ISSN: 0340-1022

PUBLISHER: Springer-Verlag

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. The synthesis, properties, and potential applications of rotaxane dendrimers, dendritic mols. containing rotaxane -like mech, bonds to link their components are described. Rotaxane dendrimers are classified into three types depending on where rotaxane-like features are introduced - Type I, II, and III rotaxane dendrimers which incorporate rotaxane -like features at the core, termini, and branches, resp. Several different types of macrocycles are employed as the ring component in the templated synthesis of rotaxane dendrimers. In the synthesis of rotaxane dendrimers, several aspects should be carefully considered, including the binding affinity of the macrocycle (ring) and quest (rod). The properties of these rotaxane dendrimers are quite different from those of the individual rotaxanes or dendrimers and often a blend of both. Potential applications of

delivery, and gene delivery.

REFERENCE COUNT: 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 7 OF 35 CAPLUS COPYRIGHT 2008 ACS on STN

rotaxane dendrimers include mol. nanoreactors, drug

ACCESSION NUMBER: 2002:449510 CAPLUS DOCUMENT NUMBER:

137:24340

TITLE: Noble gas complexes

INVENTOR(S): Mason, Rodney Stewart; Moozyckine, Alexei Uriah;

Dingley, John PATENT ASSIGNEE(S): UWS Ventures Limited, UK

SOURCE: PCT Int. Appl., 23 pp.

CODEN: PIXXD2 Patent DOCUMENT TYPE: LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT	PATENT NO. KIND DATE					APPLICATION NO.						DATE					
														-			
WO 2002				A1		2002											<
W:						AU,											
	co,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	
	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JΡ,	KΕ,	KG,	KΡ,	KR,	ΚZ,	LC,	LK,	LR,	
	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	OM,	PH,	
	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	TR,	TT,	TZ,	UA,	
	UG,	US,	UZ,	VN,	YU,	ZA,	ZM,	ZW									
RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	ΑT,	BE,	CH,	
	CY,	DE,	DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	TR,	
						CM,							ΝE,	SN,	TD,	TG	
AU 2002	0208	81		A5		2002	0618		AU 2	002-	2088	1		2	0011	204	<
PRIORITY APP	LN.	INFO	. :						GB 2	000-	2958	6		A 2	0001	204	
									GB 2	001-	9066		- 1	A 2	0010	111	
								1	WO 2	001-	GB53.	56	1	W 2	0011	204	

An infusion formulation for inducing and/or maintaining anesthesia includes a complex of a noble gas, i.e., krypton or xenon, and a mol. encapsulating agent. The encapsulating agent is a cyclodextrin, its derivative, a soluble polymer or a rotaxane. The formulation may also be used as an analgesic formulation or in a neuroprotective formulation. REFERENCE COUNT: THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 35 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:98608 CAPLUS DOCUMENT NUMBER: 136:156401

TITLE: Polyrotaxanes containing ε-polylysine as antibacterial agents, and manufacture of

ε-polvlysine therefrom

INVENTOR(S): Yui, Nobuhiko; Otani, Toru; Hiraki, Jun; Arakawa,

Kenii

PATENT ASSIGNEE(S): Chisso Corp., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.

CODEN: JKXXAF Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

DOCUMENT TYPE: PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE JP 2002037884 Α 20020206 JP 2000-226673 20000727 <--PRIORITY APPLN. INFO.: JP 2000-226673 20000727

AB The invention provides a polyrotaxane containing ε-polylysine and α-cyclodextrin, suitable for use in a food or pharmaceutical product as an antibacterial agent. Also, method fo manufacturing purified ε-polylysine by using the polyrotaxane is also disclosed.

ANSWER 9 OF 35 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2003113589 EMBASE

TITLE: Controlled release from crosslinked degradable networks.

Davis K.A.; Anseth K.S. AUTHOR:

CORPORATE SOURCE: K.S. Anseth, Department of Chemical Engineering, University

of Colorado-Boulder, Campus Box 424, Boulder, CO 80309,

United States, kristi.anseth@colorado.edu

SOURCE: Critical Reviews in Therapeutic Drug Carrier Systems,

(2002) Vol. 19, No. 4-5, pp. 385-423.

Refs: 133

ISSN: 0743-4863 CODEN: CRTSEO

United States

DOCUMENT TYPE: Journal; General Review; (Review)

FILE SEGMENT: 037 Drug Literature Index

039 Pharmacy

LANGUAGE: English

COUNTRY:

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 27 Mar 2003

Last Updated on STN: 27 Mar 2003

AB This article reviews controlled release from crosslinked degradable networks. Network formulations include those derived from wholly synthetic components, natural components, and combinations thereof. This includes, but is not limited to, poly(orthoesters), poly(anhydrides), poly(ethylene glycol) (PEG) derivatives, and dextran functional macromonomers. In addition, we present a discussion of the chemistry behind novel degradable networks with potential use in the controlled release realm.

L7 ANSWER 10 OF 35 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2002:258831 CAPLUS DOCUMENT NUMBER: 138:175631

TITLE: Multivalent interactions between biotin-polyrotaxane

conjugates and streptavidin as a model of new

targeting for transporters

AUTHOR(S): Ooya, Tooru; Yui, Nobuhiko

CORPORATE SOURCE: School of Materials Science, Japan Advanced Institute

of Science and Technology, Tatsunokuchi, Ishikawa,

923-1292, Japan

SOURCE: Journal of Controlled Release (2002),

80(1-3), 219-228

CODEN: JCREEC; ISSN: 0168-3659

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal.

LANGUAGE: English

AR Kinetic anal. of interactions between biotin-polyrotaxane or

biotin-α-cyclodextrin (biotin-α-CD) conjugates and streptavidin was carried out as a model of new targeting to transporters

using the surface plasmon resonance (SPR) technique. The biotin-polyrotaxane conjugates, in which biotin-introduced α-CDs are

threaded onto a poly(ethylene oxide) chain capped with bulky end-groups, are expected to increase the valency of biotin from monovalent to

multivalent binding. The number of biotins conjugated with one polyrotaxane mol. varied from 11 to 78, and apparently increased the association equilibrium constant (Ka), assuming pseudo-first-order kinetics. A detailed dissociation kinetics was analyzed and the re-binding of the biotin-polyrotaxane

conjugates was observed on the streptavidin-deposited SPR surface. The magnitude of the re-binding is likely to become larger with increasing the number of biotins, suggesting multivalent interaction on the SPR surface. To

quantify the effect of valency, competitive inhibition assay was performed in terms of the supramol. structure of the polyrotaxane. The inhibitory potency of the biotin-polyrotaxane conjugate was found to be 4-5 times greater than that of the biotin-a-CD conjugate. Therefore, the

biotin-polyrotaxane conjugates by supramol. formation of the biotin-a-CD conjugate significantly switches from monovalent to multivalent bindings to the model binding protein, streptavidin.

REFERENCE COUNT: THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS 29 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 11 OF 35 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:175158 CAPLUS

DOCUMENT NUMBER: 136:205279

TITLE: Biomaterials design in nano-scale sciences

AUTHOR(S): Yui, Nobuhiko

CORPORATE SOURCE: Sch. Mater. Sci., Japan Adv. Inst. Sci. Technol.,

Ishikawa, 923-1292, Japan SOURCE:

Fragrance Journal (2002), 30(1), 56-60

CODEN: FUJAD7; ISSN: 0288-9803

PUBLISHER: Fureguransu Janaru Sha DOCUMENT TYPE: Journal; General Review

LANGUAGE: Japanese

A review on design of functional materials with supramol. structure for

biomedical and pharmaceutical application, discussing design of mech. interlocked mol. assemblies such as polyrotaxanes and its application to drug delivery system, and design of biodegradable

polyrotaxane hydrogels for tissue engineering.

L7 ANSWER 12 OF 35 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 2 ACCESSION NUMBER: 2002:628383 CAPLUS

DOCUMENT NUMBER: 138:406712

TITLE: Carboxyethyl ester-polyrotaxanes as a new calcium

chelating polymer: synthesis, calcium binding and

mechanism of trypsin inhibition

AUTHOR(S): Ooya, Tooru; Eguchi, Masaru; Ozaki, Atsushi; Yui,

Nobuhiko

CORPORATE SOURCE: School of Materials Science, Japan Advanced Institute of Science and Technology, Tatsunokuchi, Ishikawa,

923-1292, Japan

SOURCE: International Journal of Pharmaceutics (2002

), 242(1-2), 47-54

CODEN: IJPHDE; ISSN: 0378-5173

PUBLISHER . Elsevier Science B.V.

DOCUMENT TYPE: Journal LANGUAGE: English

AB A carboxyethylester-polyrotaxane was synthesized as a novel calcium chelating polymer in the field of oral drug delivery

carboxyethyl ester (CEE) groups are introduced to all the primary hydroxyl groups in α -cyclodextrins (α -CDs), which are threaded onto a poly(ethylene glycol) chain capped with bulky end-groups (polyrotaxane). The solubility of the CEE-polyrotaxane in physiol. conditions increased with

pH, indicating ionization-related solubility similar to conventional polyacrylates. The ability of calcium (Ca2+) chelation was found to

and characterized in terms of mechanism of trypsin inhibition. Here,

increase in the order of poly(acrylic acid) (PAA)>CEE-

polyrotaxane»CEE-a-CD, suggesting that the increased d. of carboxyl groups enhances the Ca2+ chelating ability. The activity of

trypsin was inhibited by these compds. in the same order of the calcium chelation. However, the inhibitory effect of CEE-polyrotaxane was reduced by adding excess Ca2+ without precipitation that was observed in the presence of PAA.

Such the reduced inhibition and precipitation by CEE-a-CD was not observed Therefore, the inhibitory effect of CEE-polyrotaxane is due to Ca2+ chelation from trypsin without non-specific interaction.

REFERENCE COUNT: THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS 24 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 13 OF 35 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:691806 CAPLUS

DOCUMENT NUMBER: 138:343544

TITLE: Supramolecular design aiming at intelligent DDS

AUTHOR(S): Yui, Nobuhiko

CORPORATE SOURCE: Japan

SOURCE: Kino Zairyo (2002), 22(8), 28-34

CODEN: KIZAEP; ISSN: 0286-4835 Shi Emu Shi Shuppan PUBLISHER: DOCUMENT TYPE: Journal; General Review

LANGUAGE: Japanese

AB A review on intelligent drug delivery system (DDS).

Topics discussed are design of biomaterial containing polyrotaxane, multivalent interaction between the polyrotaxane and cell membrane receptors, design of hydrogel containing inclusion complex of α-cyclodextrin with poly(ε-lysine) and biodegradable

polyrotaxane hydrogel, and supermol. design of nano-scale biomaterial for

L7 ANSWER 14 OF 35 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:553147 CAPLUS

DOCUMENT NUMBER: 135:362419

TITLE: Polyrotaxanes with molecular recognition functions

AUTHOR(S): Oova, Tooru

CORPORATE SOURCE: Graduate School of Material Science, Hokuriku Advanced

Science and Technology University, Japan

Kobunshi (2001), 50(7), 456 SOURCE:

CODEN: KOBUA3; ISSN: 0454-1138

PUBLISHER: Kobunshi Gakkai

DOCUMENT TYPE: Journal; General Review

Japanese LANGUAGE:

AB A review with refs. A review with 19 refs., on construction and structures of polyrotaxanes with mol. recognition functions for use in

drug delivery system.

L7 ANSWER 15 OF 35 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:346895 CAPLUS

DOCUMENT NUMBER: 138:78277

TITLE: Controllable erosion time and profile in poly(ethylene glycol) hydrogels by supramolecular structure of

hydrolyzable polyrotaxane

AUTHOR(S): Ichi, T.; Lee, W. K.; Ooya, T.; Yui, N.

School of Materials Science, Japan Advanced Institute CORPORATE SOURCE:

of Science and Technology, Ishikawa, 923-1292, Japan Proceedings - 28th International Symposium on SOURCE:

Controlled Release of Bioactive Materials and 4th Consumer & Diversified Products Conference, San Diego,

CA, United States, June 23-27, 2001 (2001), Volume 1, 365-366. Controlled Release Society:

Minneapolis, Minn.

CODEN: 69CNY8

DOCUMENT TYPE: Conference LANGUAGE: English

The hydrolytic erosion behaviors of poly(ethylene glycol) (PEG) hydrogels crosslinked by a hydrolyzable polyrotaxane were characterized. The erosion time and profile of these hydrogels were controllable and these hydrogels showed the enhanced stability of hydrolysis with highly water

swollen state.

REFERENCE COUNT: THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 16 OF 35 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:670733 CAPLUS

DOCUMENT NUMBER: 136:345631

TITLE: Synthesis of polyrotaxane-biotin conjugates and

surface plasmon resonance analysis of streptavidin

recognition

AUTHOR(S): Ooya, Tooru; Kawashima, Tomokatsu; Yui, Nobuhiko CORPORATE SOURCE: School of Materials Science, Japan Advanced Institute

of Science and Technology, Ishikawa, 923-1292, Japan Biotechnology and Bioprocess Engineering (2001 SOURCE:

), 6(4), 293-300

CODEN: BBEIAU; ISSN: 1226-8372

PUBLISHER: Korean Society for Biotechnology and Bioengineering

DOCUMENT TYPE: Journal LANGUAGE: English

A polyrotaxane-biotin conjugate was synthesized and its interaction with streptavidin measured using surface plasmon resonance (SPR) detection. A

biodegradable polyrotaxane in which .apprx.22 mols. of

α-cvclodextrins (α-CDs) were threaded onto a polv(ethylene oxide) chain (Mn: 4,000) capped with benzyloxycarbonyl-L-phenylalanine was conjugated with a biotin hydrazide and 2-aminoethanol after activating the

hydroxyl groups of α -CDs in the polyrotaxane using N,N'-carbonyldiimidazole. The results of the high-resolution 1H-NMR (1H-NMR) spectra and gel permeation chromatog. of the conjugate showed that

.apprx.11 biotin mols. were actually introduced to the polyrotaxane scaffold. An SPR anal. showed that the binding curves of the biotin mols.

in the conjugate on the streptavidin-deposited surface changed in a

concentration

dependent manner, indicating that the biotin in the conjugate was actually recognized by streptavidin. The association equilibrium constant (Ka) of the interaction between the conjugate and streptavidin tetramer was of the order 107. These results suggest that polyrotaxane is useful for scaffolds as a polymeric ligand in biomedical fields.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 17 OF 35 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:825190 CAPLUS

DOCUMENT NUMBER: 137:98696

TITLE: Biodegradable polyrotaxanes aiming at biomedical and pharmaceutical applications Ooya, Tooru; Yui, Nobuhiko

AUTHOR(S): CORPORATE SOURCE: Japan Advanced Institute of Science and Technology,

School of Materials Science, Ishikawa, 923-1292, Japan Biomedical Polymers and Polymer Therapeutics. SOURCE:

[Proceedings of the International Symposium on Frontiers in Biomedical Polymers Including Polymer Therapeutics: From Laboratory to Clinical Practice], 3rd, Biwa Lake, Japan, May 23-27, 1999 (2001

), Meeting Date 1999, 75-90. Editor(s): Chiellini, Emo. Kluwer

Academic/Plenum Publishers: New York, N. Y. CODEN: 69BZMR

DOCUMENT TYPE: Conference; General Review

LANGUAGE:

English

A review on the design of biodegradable polyrotaxanes as a novel candidate for drug carriers as well as implantable materials for tissue engineering. Poly(ethylene glycol) and α-cyclodextrin were used as main

components of the polyrotaxane. The supramol. structure and dissociation of the polyrotaxanes will be the most unique characteristics when considering biomedical and pharmaceutical applications.

REFERENCE COUNT: THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS 39 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 18 OF 35 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:704221 CAPLUS

DOCUMENT NUMBER: 136:406652

TITLE: Bio-material design aiming at polyrotaxane structure

AUTHOR(S): Yui, Nobuhiko; Ooya, Tooru

CORPORATE SOURCE: Graduate School of material Science, Japan Advanced

Institute of Science and Technology, Japan

SOURCE: Mirai Zairyo (2001), 1(3), 26-32

CODEN: MZIABA

PUBLISHER: Enu-Ti-Esu

DOCUMENT TYPE: Journal; General Review

LANGUAGE: Japanese

AB A review. This article reviews the potential of polyrotaxane in drug delivery system and tissue engineering with the

description of their unique structure properties.

ANSWER 19 OF 35 CAPLUS COPYRIGHT 2008 ACS on STN ACCESSION NUMBER: 2000:846509 CAPLUS

DOCUMENT NUMBER: 134:183381

TITLE: Synthesis and characterization of an

oligopeptide-terminated polyrotaxane as a drug carrier

Ooya, Tooru; Arizono, Koichi; Yui, Nobuhiko AUTHOR(S):

CORPORATE SOURCE: School of Materials Science, Japan Advanced Institute

of Science and Technology, Ishikawa, 923-1292, Japan Polymers for Advanced Technologies (2000). SOURCE:

11(8-12), 642-651

CODEN: PADTE5; ISSN: 1042-7147

John Wiley & Sons Ltd. PUBLISHER:

DOCUMENT TYPE: Journal

LANGUAGE: English

A polyrotaxane consisting of α -cyclodextrins (α -CDs) and

α, ω-di(glycylglycyne) polyoxyethylene (α, ω-di(Gly-

Gly)-PEG) capped with tyrosine was synthesized as a drug carrier and its

in vitro degradation by aminopeptidase M was demonstrated. α, ω-Di(Gly-Gly)-PEG was prepared by condensation reaction between terminal amino-groups in α-(3-aminopropy1)-ω-(3-

aminopropyl) polyoxyethylene and succinimide ester of N-tert-

butyloxycarbonyl (Boc)-Gly-Gly, followed by the deprotection of Boc group via acidic hydrolysis. A polypseudorotaxane consisting of α -CDs and

α, ω-di(Gly-Gly)-PEG was prepared in the mixture of water and dimethylsulfoxide. The polyrotaxane was successfully synthesized by condensation reaction between the amino-groups in the pseudopolyrotaxane and p-nitrophenyl ester of carbobenzoxy L-tyrosine. The addition of 1-hydroxy-1H-benzotriazole on the reaction was found to increase the yield and the number of α -CDs in the polyrotaxane. Hydroxypropylation of the polyrotaxane improved the solubility in aqueous solns, and many kinds of organic

solvents. In vitro degradation of the hydroxypropylated (HP-)polyrotaxane revealed that $HP-\alpha$ -CDs in the HP-polyrotaxane were released in the presence of aminopeptidase M. These results suggest that the supramol. dissociation will be triggered by the action of extra-cellular enzymes and lead to a new mechanism of drug release from polymeric drug carriers. REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 20 OF 35 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:341389 CAPLUS

DOCUMENT NUMBER: 133:139965

TITLE: Supramolecular-structured polymers for drug

AUTHOR(S):

delivery Oova, Tooru; Yui, Nobuhiko

CORPORATE SOURCE: School of Materials Science, Japan Advanced Institute of Science and Technology, Ishikawa, 923-1292, Japan

ACS Symposium Series (2000), 752(Controlled

SOURCE:

Drug Delivery), 375-384 CODEN: ACSMC8; ISSN: 0097-6156

American Chemical Society

PUBLISHER: DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

A review, with 25 refs. Polyrotaxanes as a supramol.-structured polymer were characterized aiming at a drug carrier, a drug permeation enhancer, an implantable material, and a stimuli-responsive material. Biodegradable polyrotaxanes exhibit their supramol. architectures: many

 α -cyclodextrins (α -CDs) are threaded onto a single

poly(ethylene glycol) (PEG) chain capped with biodegradable bulky end-groups. Further, a stimuli-responsive polyrotaxane, in which many

β-CDs are threaded onto a triblock-copolymer of PEG and

poly(propylene glycol) (PPG) capped with fluorescein-4-isothiocyanate, was designed as a novel smart material.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 21 OF 35 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:331609 CAPLUS

TITLE: Peptide rotaxanes as potential drug

delivery systems. AUTHOR(S): Leigh, David A.; van Meurs, Sandra; Slater, Martin J.;

Murphy, Aden

CORPORATE SOURCE: Centre for Supramolecular and Macromolecular

Chemistry, University of Warwick, Coventry, CV4 7AL,

UK

Book of Abstracts, 219th ACS National Meeting, San SOURCE: Francisco, CA, March 26-30, 2000 (2000),

MEDI-008. American Chemical Society: Washington, D.

C.

CODEN: 69CLAC

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

The discovery of a simple hydrogen bonding template for rotaxane formation has led to investigations into the potential of using rotaxanes of biol. active peptides as novel drug

delivery systems. Here we describe how rotaxane formation imparts enzyme stability upon the peptide and how manipulation

of the solubility and transport properties can be achieved through

functionalisation of the rotaxane macrocycle.

L7 ANSWER 22 OF 35 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

ACCESSION NUMBER: 2000:222509 BIOSIS DOCUMENT NUMBER: PREV200000222509

TITLE: Peptide rotaxanes as potential drug

delivery systems.

AUTHOR(S): Leigh, David A. [Reprint author]; van Meurs, Sandra

[Reprint author]; Slater, Martin J.; Murphy, Aden [Reprint

author]
CORPORATE SOURCE: Centre for Supramolecular and Macromolecular Chemistry,

Department of Chemistry, University of Warwick, Gibbet Hill

Road, Coventry, CV4 7AL, UK

SOURCE: Abstracts of Papers American Chemical Society, (

2000) Vol. 219, No. 1-2, pp. MEDI 8. print.

Meeting Info.: 219th Meeting of the American Chemical Society. San Francisco, California, USA. March 26-30, 2000.

American Chemical Society. CODEN: ACSRAL. ISSN: 0065-7727.

DOCUMENT TYPE: Conference: (Meeting)

Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 31 May 2000

Last Updated on STN: 5 Jan 2002

L7 ANSWER 23 OF 35 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:453602 CAPLUS

DOCUMENT NUMBER: 132:69125

TITLE: Polyrotaxanes: synthesis, structure, and potential in

drug delivery

AUTHOR(S): Ooya, Tooru; Yui, Nobuhiko

CORPORATE SOURCE: School of Materials Science, Japan Advanced Institute of Science and Technology, Ishikawa, 923-1292, Japan

Critical Reviews in Therapeutic Drug Carrier Systems (1999), 16(3), 289-330

CODEN: CRTSEO; ISSN: 0743-4863

PUBLISHER: Begell House, Inc.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

SOURCE:

AB This article reviews with 91 refs. the potential of polyrotaxanes in

drug delivery with the historical background of polyrotaxanes, syntheses. Pseudopolyrotaxanes and polyrotaxanes, including classifications, synthetic methods, structures and phys. properties are discussed in the first section. The second section provides our concept of drug carriers using drug-polyrotaxane conjugates in comparison with conventional drug-polymer conjugates. The third and fourth sections describe the synthetic method for biodegradable polyrotaxanes, the conjugation with drugs, and their association under physiol. conditions. The

fifth section discusses other possibilities for the polyrotaxanes such as drug penetration enhancers. These studies suggest the potential of polyrotaxanes in pharmaceutical applications.

REFERENCE COUNT: 91 THERE ARE 91 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 24 OF 35 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:653460 CAPLUS

DOCUMENT NUMBER: 132:141754

TITLE: Biodegradable polyrotaxanes as a drug carrier

AUTHOR(S): Ooya, T.; Yui, N.

CORPORATE SOURCE: School of Materials Science, Japan Advanced Institute of Science and Technology, Ishikawa, 923-1292, Japan

S.T.P. Pharma Sciences (1999), 9(1), 129-138 SOURCE:

CODEN: STSSE5; ISSN: 1157-1489

PUBLISHER: Editions de Sante DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

A review with 51 refs. This article reviews our concept of drug delivery systems using drug/polyrotaxane conjugates as drug carriers. The biodegradable polyrotaxanes exhibit their supramol. architectures: many α -cyclodextrins are threaded onto a single poly(ethylene glycol) chain capped with biodegradable bulky end-groups. The synthetic method of the polyrotaxanes, the conjugation with drugs, and their association nature in a physiol. condition are described. The supramol. dissociation of the drug/polyrotaxane conjugates via terminal peptide cleavage by a hydrolytic enzyme is discussed in relation

to their association nature. Through these studies, advantages of drug/polyrotaxane conjugates as drug carriers are suggested in comparison with conventional drug/polymer conjugates.

THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: 51 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 25 OF 35 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:539755 CAPLUS

TITLE: Peptido[2]rotaxanes with oligosaccharide

stoppers: A model system for controlled peptide

drug delivery.

AUTHOR(S): Leigh, David A.; Nepogodiev, Sergey A.

CORPORATE SOURCE: Department of Chemistry, University of Warwick,

Coventry, CV4 7AL, UK

Book of Abstracts, 218th ACS National Meeting, New SOURCE:

Orleans, Aug. 22-26 (1999), CARB-022. American Chemical Society: Washington, D. C.

CODEN: 67ZJA5

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

For efficient application as drugs, potent oligopeptides must overcome a number of phys. and enzymic barriers presented. Amongst these are the susceptibility of peptides to the action of hydrolytic enzymes and their poor membrane transport properties. Temporary encapsulation of peptides by a macrocycle in the form of [2]rotaxanes is proposed as a possible solution to these problems. For application as a drug delivery systems one of the stoppers attached to the end of oligopeptide thread should be degradable under physiol. conditions allowing the 'slippage' of the macrocycle. We investigated the application of oligosaccharides as biodegradable stoppers for [2] rotaxanes based on GlyGly. [2]Rotaxanes 1 and 2a were prepared through the 'clipping' strategy. After deprotection of the sugar portions of these compds. only rotaxane 2b was stable. The disassembling of 2b can be achieved through the action of a-mannosidases.

ANSWER 26 OF 35 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on SIN

ACCESSION NUMBER: 1999:412609 BIOSIS DOCUMENT NUMBER: PREV199900412609

TITLE: Peptido(2)rotaxanes with oligosaccharide

stoppers: A model system for controlled peptide drug delivery.

Leigh, David A. [Reprint author]; Nepogodiev, Sergey A. AUTHOR(S):

[Reprint author]

CORPORATE SOURCE: Department of Chemistry, University of Warwick, Coventry,

CV4 7AL, UK

SOURCE: Abstracts of Papers American Chemical Society, (

1999) Vol. 218, No. 1-2, pp. CARB 22. print.

Meeting Info.: 218th National Meeting of the American Chemical Society, Parts 1 and 2. New Orleans, Louisiana,

USA. August 22-26, 1999. American Chemical Society.

CODEN: ACSRAL. ISSN: 0065-7727.

DOCUMENT TYPE: Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 8 Oct 1999

Last Updated on STN: 8 Oct 1999

L7 ANSWER 27 OF 35 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:666077 CAPLUS

DOCUMENT NUMBER: 129:331307

TITLE: Supramolecular dissociation of biodegradable polyrotaxanes by enzymic terminal hydrolysis

AUTHOR(S): Ooya, Tooru; Yui, Nobuhiko

CORPORATE SOURCE: School Materials Sci., Japan Advanced Inst. Sci.

Technol., Ishikawa, 923, Japan

SOURCE: Macromolecular Chemistry and Physics (1998), 199(10), 2311-2320

CODEN: MCHPES; ISSN: 1022-1352

PUBLISHER: Huethig & Wepf Verlag

DOCUMENT TYPE: Journal LANGUAGE: English

AB Supramol. dissociation of biodegradable polyrotaxanes via terminal hydrolysis by an enzyme (papain) in vitro was investigated in relation to their solution

properties. The polyrotaxanes were synthesized by the introduction of L-phenylalanine (L-Phe) at both ends of an inclusion complex consisting of a-cyclodextrins (a-CDs) and amino-terminated poly(ethylene

glycol) (PEG) via peptide linkages, followed by the hydroxypropylation of α -CDs. From static and dynamic light scattering studies, it was clarified that the polyrotaxanes form a loosely packed association but

LePhe-terminated PEGs form a tightly packed association Further, the polyrotaxanes were found to maintain their rod-like structures in physiol. conditions. In vitro degradation expts. using papain revealed that the terminal hydrolysis of the polyrotaxanes is completed and accompanied by

the release of hydroxypropylated α -CDs, and this behavior is not affected by the association number of the polyrotaxanes. On the other hand,

the

terminal hydrolysis of L-Phe-terminated PEG is limited under similar conditions. From these results, the complete dissociation of the polyrotaxanes by hydrolysis is considered to be due to the loosely packed association, presumably related to the rod-like structure. The potential for drug delivery is discussed.

L7 ANSWER 28 OF 35 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1997:664215 CAPLUS

DOCUMENT NUMBER: 127:351269

TITLE: Transdermal absorption accelerators and their preparation

INVENTOR(S): Yui, Nobuhiko
PATENT ASSIGNEE(S): Yui, Nobuhiko, Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.

CODEN: JKXXAF
DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE JP 09263547 JP 3704194 A 19971007 JP 1996-76491 19960329 <--B2 20051005

PRIORITY APPLN. INFO.: JP 1996-76491 19960329

AB The title accelerators comprise several hydroxypropylated α -, β-, or γ-cyclodextrin mols. whose cavities are occupied by biodegradable group-terminated linear macromols., and are prepared by (A) treatment of Z-L-Phe with N-hydroxysuccinimide (N-HOSu), (B) addition of a, m-di(3-aminopropyl)-polyoxyethylene to an aqueous cyclodextrin solution, (C) addition of the resulting pseudopolyrotaxane to a solution of Z-L-Phe-OSu obtained in the process A, (D) hydroxypropylation of the resulting Z-L-Phe-polyrotaxane, and optional (E) deprotection of the Z group by reduction The accelerators cause no cytotoxicity, skin irritation, or inflammation. Hydroxypropylated Z-L-Phe-polyrotaxane significantly enhanced transdermal absorption of indomethacin in isolated rat skin.

L7 ANSWER 29 OF 35 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1997:664211 CAPLUS

DOCUMENT NUMBER: 127:351268

TITLE: Indomethacin topical preparations containing

biodegradable polymer assembly having supramolecular

structure Yui, Nobuhiko

INVENTOR(S): PATENT ASSIGNEE(S): Toko Yakuhin Kogyo K. k., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.

CODEN: JKXXAF DOCUMENT TYPE: Patent LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 09263535	A	19971007	JP 1996-76490	19960329 <
JP 3830198	B2	20061004		
RIORITY APPLN. INFO.:			JP 1996-76490	19960329

AB The topical preparation contains indomethacin (I) and a biodegradable polymer assembly having a supramol. structure which comprises a number of α -, β-, or γ-cyclodextrin, a linear polymer penetrating through the hollows of the cyclodextrins, and biodegradable moieties bonded to both ends of the polymer. The unique polymer assembly improves transdermal absorption of drugs without causing skin irritation and toxicity. A saturated α-cyclodextrin solution was treated with PEG 4000BA $[\alpha - (3-\text{aminopropyl}) - \omega - (3-\text{aminopropoxy}) \text{ poly}(\text{oxyethylene})]$ and the resulting turbid solution was ultrasonicated then let stand overnight to give a pseudopolyrotaxane comprising 35-40 cyclodextrin mols. and a threading polyoxyethylene chain. The pseudopolyrotaxane was treated with a DMS solution of Z-L-Phe-Su, prepared from carbobenzoxy-L-phenylalanine and N-hydroxysuccinimide, to give Z-L-Phe-polyrotaxane. This was hydroxypropylated with propylene oxide, followed by deprotection of carbobenzoxy group. Permeation of I through a sheet of hairless mouse skin pretreated with the hydroxypropylated polyrotaxane was 19.27 μg/cm3 for 8 h, vs. 9.10 μg/cm3 for a control using H2O as pretreatment agent.

L7 ANSWER 30 OF 35 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1997:463672 CAPLUS DOCUMENT NUMBER: 127:126414

TITLE: Peptide-biodegradable polyrotaxane conjugate as a

peptide delivery system Ooya, Tooru; Yui, Nobuhiko

AUTHOR(S):

CORPORATE SOURCE: Japan Advanced Institute of Science and Technology,

Tatsunokuchi, 923-12, Japan

SOURCE: Proceedings of the International Symposium on

Controlled Release of Bioactive Materials (

1997), 24th, 459-460

CODEN: PCRMEY; ISSN: 1022-0178

PUBLISHER: Controlled Release Society, Inc.

DOCUMENT TYPE: Journal LANGUAGE: English

AB A peptide conjugate with supramol. assembly was prepared, and physicochem. stability was evaluated. The conjugate has supramol. structure and 2 amino groups of insulin were modified. Further, conformational change of insulin was prevented by the modification. It is suggested that his supramol. conjugate is feasible as a peptide drug carrier.

L7 ANSWER 31 OF 35 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1997:339997 CAPLUS

DOCUMENT NUMBER: 127:70694

TITLE: Synthesis and characterization of biodegradable

polyrotaxane as a novel supramolecular-structured drug

carrier

AUTHOR(S): Ooya, Tooru; Yui, Nobuhiko

CORPORATE SOURCE: School of Materials Science, Japan Advanced Institute

of Science and Technology, Tatsunokuchi, Ishikawa,

923-12, Japan

SOURCE: Journal of Biomaterials Science, Polymer Edition (

Polyrotaxanes were synthesized as novel biodegradable polymers with supramol, assembly and their properties evaluated in vitro. The synthesis

1997), 8(6), 437-455 CODEN: JBSEEA; ISSN: 0920-5063

PUBLISHER: VSP

DOCUMENT TYPE: Journal LANGUAGE: English

of biodegradable polyrotaxanes consists of three steps: preparation of an inclusion complex consisting of α -cyclodextrins (α -CDs) and amino-terminated poly(ethylene glycol) (PEG); introduction of L-phenylalanine (L-Phe) at each complex terminal via peptide linkages; and hydroxypropylation of α -CDs in the polyrotaxanes. Succinimide ester of benzyloxycarbonyl-L-Phe was condensed with the terminal amino groups of the inclusion complex. IH-IMPR and GFC results showed that α -CDs were threaded onto a PEG chain and L-Phe moieties were introduced at each terminal of the PEG chain. Further, the amount of threaded α -CDs was found to be governed by the mol. weight of PEG. The hydroxypropylation of α -CDs improved the solubility of the polyrotaxanes in PES (pH 7.4). The hydroxypropylated (HP-) polyrotaxanes were characterized by terminal peptide cleavage using papain. In vitro degradation of HP-polyrotaxanes revealed that HP- α -CDs threaded onto a PEG chain were released only when terminal peptide linkages were cleaved.

were found to be independent of the mol. weight of HP-polyrotaxanes but to be affected by terminal hydrophobic moieties. It is proposed that our designed polyrotaxanes are feasible as novel drug carriers.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

HP-a-CDs chain were released only when terminal peptide linkages were cleaved. Moreover, threaded HP-a-CDs onto a PEG chain was found to be completely released. Kinetics of terminal peptide cleavage were also evaluated by catalytic efficiency (kcat/Km). The kcat/Km values

L7 ANSWER 32 OF 35 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1997:117230 CAPLUS

DOCUMENT NUMBER: 126:229499

TITLE: Interaction of supramolecular assembly with hairless

rat stratum corneum

AUTHOR(S): Kamimura, Wataru; Ooya, Tooru; Yui, Nobuhiko CORPORATE SOURCE: Sch. Mater. Sci., Japan Ad. Inst. Sci. Technol.,

Ishikawa, 923-12, Japan

SOURCE: Journal of Controlled Release (1997),

44(2,3), 295-299

CODEN: JCREEC; ISSN: 0168-3659
PUBLISHER: Elsevier

DOCUMENT TYPE: Journal LANGUAGE: English

AB Polyrotaxanes are well known as a supramol. assembly in which many cyclic compds are threaded onto a linear polymeric chain capped with bulky end-groups. In this paper, a polyrotaxane consisting of a-CDs and PEG capped with biodegradable peptide moieties was synthesized, and the interaction with stratum corneum of hairless rat skin was examined by means of a differential scanning calorimetry. The hydroxypropylated polyrotaxane was found to interact with lipid components in the stratum corneum: bound water content was significantly decreased although ordered lipid bilayers were maintained. Thus, it is suggested that our designed polyrotaxane can be feasible as novel candidates for transdermal penetration enhancers.

L7 ANSWER 33 OF 35 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1996:377201 CAPLUS

DOCUMENT NUMBER: 125:41804

TITLE: Biodegradable medicinal polymer assembly with

supermolecular structure

INVENTOR(S): Yui, Nobuhiko

PATENT ASSIGNEE(S): Japan

SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA'	TENT :	NO.			KIN	D :	DATE			APPL	ICAT	ION :	NO.		D.	ATE		
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EP	7308	69			A1		1996	0911		EP 1	995-	9181	78		1	9950	512	<
EP	7308	69			B1		2001	0627										
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										WO 1	995-	JP90	9		W 1	9950	512	

AB The invention relates to a highly water-soluble polymer having arbitrarily controllable drug-carrying capacity and drug-releasing characteristics and serving as a novel drug carrier widely applicable in vivo; and a biodegradable medicinal polymer assembly having a supermol. structure and being capable of releasing a drug in response to a specific biodegradn.

occurring in each disease. The assembly comprises a number of drug-carrying cyclic compds. prepared by binding a drug to α , β or Y-cyclodextrin, a linear polymer penetrating through the hollows of the cyclic compds., and biodegradable moieties bonded to both ends of the polymer. A biodegradable medicinal polymer assembly with supermol. structure for mitomycin C delivery is given as an example.

L7 ANSWER 34 OF 35 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1996:489035 CAPLUS

DOCUMENT NUMBER: 125:177188

TITLE: Novel design of supramolecular-structured

biodegradable polymer for drug

delivery

AUTHOR(S): Yui, Nobuhiko; Ooya, Tooru

CORPORATE SOURCE: Sch. Materials Science, JAIST, Ishikawa, 923-12, Japan SOURCE:

Advanced Biomaterials in Biomedical Engineering and Drug Delivery Systems, [Iketani Conference on Biomedical Polymers], 5th, Kagoshima, Japan, Apr.

18-22, 1995 (1996), Meeting Date 1995, 333-334. Editor(s): Ogata, Naoya. Springer: Tokyo,

Japan.

CODEN: 63CXA6 DOCUMENT TYPE: Conference

LANGUAGE: English

Biodegradable polymers with supramol. structures were proposed as a novel candidate of substrates for temporal drug delivery. A biodegradable polyrotaxane was synthesized in which α-cyclodextrins (α-CDs) as drug carriers were threaded onto a poly(ethylene glycol) (PEG) chain capped at each terminal with L-phenylalanine (L-Phe) via peptide linkages. The release of α-CDs from the biodegradable polyrotaxane was observed only when the terminal peptide linkages were hydrolyzed by papain. Further, the dethreading process of α -CDs from PEG chains was also observed to be quite rapid. Therefore, it is suggested that α -CD release from the biodegradable polyrotaxane was controlled by the hydrolysis of terminal peptide linkages.

ANSWER 35 OF 35 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1996:267862 CAPLUS DOCUMENT NUMBER: 125:41536

TITLE: Biodegradable polyrotaxanes for drug

deliverv

AUTHOR(S): Yui, Nobuhiko CORPORATE SOURCE: Grad, Sch., Hokuniku Univ., Japan

SOURCE: Kobunshi (1996), 45(4), 263 CODEN: KOBUA3; ISSN: 0454-1138

PUBLISHER: Kobunshi Gakkai

DOCUMENT TYPE: Journal; General Review

LANGUAGE: Japanese

AB A review with 5 refs. discussing biodegradable polyrotaxanes for use in drug delivery systems.

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L10 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2008 ACS on STN
ΔM
    2003:717792 CAPLUS
DN
    139:224476
TI Multivalently interactive molecular assembly, capturing agent, drug
    carrier, calcium chelating agent, and drug enhancer
IN Yui, Nobuhiko; Maruyama, Atsushi; Ooya, Tooru
PA Japan
SO U.S. Pat. Appl. Publ., 33 pp.
    CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2
     PATENT NO.
                   KIND DATE APPLICATION NO. DATE
                         ----
PI US 2003171573 A1 20030911 US 2002-230394 
JP 2004027183 A 20040129 JP 2003-51163 
US 2004162275 A1 20040819 US 2003-679499 
PRAI JP 2002-24744 A 20020227 
US 2002-230394 A 20020829
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L11 34 ROTAXANE (S) DRUG

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L13 ANSWER 1 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:681395 CAPLUS

DOCUMENT NUMBER: 141:195314

TITLE: Multivalently interactive molecular assembly, capturing agent, drug carrier, calcium chelating

agent, and drug enhancer
INVENTOR(S): Yui, Nobuhiko: Maruyama.

INVENTOR(S): Yui, Nobuhiko; Maruyama, Atsushi; Ooya, Tooru PATENT ASSIGNEE(S): Japan

SOURCE: U.S. Pat. Appl. Publ., 47 pp., Cont.-in-part of U.S. Pat. Appl. 2003 171,573.

CODEN: USXXCO
DOCUMENT TYPE: Patent

LANGUAGE: English FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004162275	A1	20040819	US 2003-679499	20031007
US 2003171573	A1	20030911	US 2002-230394	20020829 <
PRIORITY APPLN. INFO.:			JP 2002-52474 A	20020227
			HS 2002-230394 B	2 20020829

AB A multivalently interactive mol. assembly having a plurality of functional groups or ligands, in which a ratio between Rh and Rg expressed as Rh/Rg is 1.0 or less. Here, Rh is a hydrodynamic radius calculated from dynamic light scattering (DLS) assay performed in aqueous solution; and Rg is a radius of

gyration determined based on the Zimm plot generated using data obtained by static light scattering (SLS) assay. A polyrotaxane was prepared from $\alpha-\text{cyclodextrin}$ and diamino-PEG and reacted with Z-L-Phe succinimide ester. Then biotin mols. were introduced into the polyrotaxane mol.

Examples were given of anal. of biotin-polyrotaxane conjugate binding to streptavidin-immobilized surface using surface plaanance. Trypsin activity inhibition and Ca chelating activities of polyrotaxanes were also given.

L13 ANSWER 2 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:819708 CAPLUS DOCUMENT NUMBER: 140:391507

TITLE: Rotaxane dendrimers
AUTHOR(S): Lee, Jae Wook; Kim, Kimoon

CORPORATE SOURCE: Department of Chemistry, Dong-A University, Pusan,

604-714, S. Korea
SOURCE: Topics in Current Chemistry (2003),

228 (Dendrimers V), 111-140
CODEN: TPCCAQ; ISSN: 0340-1022

PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

ARANOME:

A review. The synthesis, properties, and potential applications of rotaxane dendrimers, dendritic mols. containing rotaxane-like mech. bonds to link their components are described. Rotaxane dendrimers are classified into three types depending on where rotaxane-like features are introduced - Type I, II, and III rotaxane dendrimers which incorporate rotaxane-like features at the core, termini, and branches, resp. Several different types of macrocycles are employed as the ring component in the templated synthesis of rotaxane dendrimers. In the synthesis of rotaxane dendrimers are describly considered, including the binding affinity of the macrocycle (ring) and guest (rod). The properties of these rotaxane dendrimers are quite different from those of the individual rotaxanes or dendrimers and often a blend of both. Potential

drug delivery, and gene delivery.

REFERENCE COUNT: 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:717792 CAPLUS

DOCUMENT NUMBER: 139:224476

TITLE: Multivalently interactive molecular assembly, capturing agent, drug carrier, calcium chelating

applications of rotaxane dendrimers include mol. nanoreactors,

agent, and drug enhancer
INVENTOR(S): Yui, Nobuhiko; Maruyama, Atsushi; Ooya, Tooru

PATENT ASSIGNEE(S): Japan

SOURCE: U.S. Pat. Appl. Publ., 33 pp.

DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003171573	A1	20030911	US 2002-230394	20020829 <
JP 2004027183	A	20040129	JP 2003-51163	20030227
US 2004162275	A1	20040819	US 2003-679499	20031007
PRIORITY APPLN. INFO.:			JP 2002-52474 A	. 20020227
			HS 2002-230394 A	20020829

AB The invention relates to a multivalently interactive mol. assembly which can effectively and stably bind to a target substance in vivo or in vitro, a capturing agent comprising said multivalently interactive mol. assembly for capturing an object of interest in vivo or in vitro, a drug carrier which aids administration of a drug, a calcium chelating agent which can

effectively chelate calcium, and a drug enhancer which can be administered with a drug to assist in e.g. absorption of the drug. The invention discloses a multivalently interactive mol. assembly having a plurality of functional groups or ligands, in which a ratio between Rh and Rg expressed as Rh/Rg is 1.0 or less. Here, Rh is a hydrodynamic radius calculated from a dynamic light scattering assay performed in aqueous solution, and Rq is a radius

of gyration determined based on the Zimm plot generated using data obtained by a static light scattering assay. Specifically, the invention discloses polyrotaxanes, the synthesis of which is described.

L13 ANSWER 4 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:691806 CAPLUS

DOCUMENT NUMBER: 138:343544

TITLE: Supramolecular design aiming at intelligent DDS

AUTHOR (S): Yui, Nobuhiko

CORPORATE SOURCE: Japan Kino Zairyo (2002), 22(8), 28-34

SOURCE: CODEN: KIZAEP; ISSN: 0286-4835

PUBLISHER: Shi Emu Shi Shuppan DOCUMENT TYPE: Journal; General Review

LANGUAGE: Japanese

A review on intelligent drug delivery system (DDS). Topics discussed are design of biomaterial containing polyrotaxane, multivalent interaction between the polyrotaxane and cell membrane receptors, design of hydrogel containing inclusion complex of α -cyclodextrin with poly(ϵ -lysine) and

biodegradable polyrotaxane hydrogel, and supermol. design of nano-scale biomaterial for DDS.

L13 ANSWER 5 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:553147 CAPLUS DOCUMENT NUMBER: 135:362419

TITLE: Polyrotaxanes with molecular recognition functions

AUTHOR(S): Ooya, Tooru

CORPORATE SOURCE: Graduate School of Material Science, Hokuriku Advanced

Science and Technology University, Japan

SOURCE: Kobunshi (2001), 50(7), 456

CODEN: KOBUA3; ISSN: 0454-1138

PUBLISHER: Kobunshi Gakkai DOCUMENT TYPE: Journal; General Review

LANGUAGE: Japanese

AB A review with refs. A review with 19 refs., on construction and structures of polyrotaxanes with mol. recognition functions for use in

drug delivery system.

L13 ANSWER 6 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:846509 CAPLUS

DOCUMENT NUMBER: 134:183381

TITLE: Synthesis and characterization of an

oligopeptide-terminated polyrotaxane as a drug carrier

Ooya, Tooru; Arizono, Koichi; Yui, Nobuhiko AUTHOR(S):

CORPORATE SOURCE: School of Materials Science, Japan Advanced Institute of Science and Technology, Ishikawa, 923-1292, Japan

SOURCE: Polymers for Advanced Technologies (2000),

11(8-12), 642-651

CODEN: PADTE5; ISSN: 1042-7147

PUBLISHER: John Wiley & Sons Ltd.

DOCUMENT TYPE: Journal LANGUAGE: English

A polyrotaxane consisting of α -cyclodextrins (α -CDs) and AB

α, ω-di(glycylglycyne) polyoxyethylene (α, ω-di(Gly-Gly)-PEG) capped with tyrosine was synthesized as a drug carrier and its

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in vitro degradation by aminopeptidase M was demonstrated.
     α, ω-Di(Gly-Gly)-PEG was prepared by condensation reaction
     between terminal amino-groups in α-(3-aminopropyl)-ω-(3-
     aminopropyl) polyoxyethylene and succinimide ester of N-tert-
     butyloxycarbonyl (Boc)-Gly-Gly, followed by the deprotection of Boc group
     via acidic hydrolysis. A polypseudorotaxane consisting of \alpha-CDs and
     α, ω-di(Gly-Gly)-PEG was prepared in the mixture of water and
     dimethylsulfoxide. The polyrotaxane was successfully synthesized by
     condensation reaction between the amino-groups in the pseudopolyrotaxane
     and p-nitrophenyl ester of carbobenzoxy L-tyrosine. The addition of
     1-hydroxy-1H-benzotriazole on the reaction was found to increase the yield
     and the number of \alpha-CDs in the polyrotaxane. Hydroxypropylation of the
     polyrotaxane improved the solubility in aqueous solns. and many kinds of
organic
     solvents. In vitro degradation of the hydroxypropylated (HP-)polyrotaxane
     revealed that HP-α-CDs in the HP-polyrotaxane were released in the
     presence of aminopeptidase M. These results suggest that the supramol.
     dissociation will be triggered by the action of extra-cellular enzymes and
     lead to a new mechanism of drug release from polymeric drug carriers.
REFERENCE COUNT:
                               THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS
                         33
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L13 ANSWER 7 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:
                         2000:341389 CAPLUS
DOCUMENT NUMBER:
                         133:139965
TITLE:
                         Supramolecular-structured polymers for drug delivery
AUTHOR(S):
                        Ooya, Tooru; Yui, Nobuhiko
CORPORATE SOURCE:
                        School of Materials Science, Japan Advanced Institute
                        of Science and Technology, Ishikawa, 923-1292, Japan
SOURCE .
                         ACS Symposium Series (2000), 752(Controlled
                         Drug Delivery), 375-384
                         CODEN: ACSMC8; ISSN: 0097-6156
PUBLISHER:
                         American Chemical Society
DOCUMENT TYPE:
                         Journal; General Review
LANGUAGE:
                         English
   A review, with 25 refs. Polyrotaxanes as a supramol.-structured polymer
     were characterized aiming at a drug carrier, a drug permeation enhancer,
     an implantable material, and a stimuli-responsive material. Biodegradable
     polyrotaxanes exhibit their supramol. architectures: many
     α-cyclodextrins (α-CDs) are threaded onto a single
     polv(ethylene glycol) (PEG) chain capped with biodegradable bulky
     end-groups. Further, a stimuli-responsive polyrotaxane, in which many
     β-CDs are threaded onto a triblock-copolymer of PEG and
     poly(propylene qlycol) (PPG) capped with fluorescein-4-isothiocyanate, was
     designed as a novel smart material.
REFERENCE COUNT:
                         25
                               THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L13 ANSWER 8 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:
                         2000:331609 CAPLUS
TITLE:
                         Peptide rotaxanes as potential drug
                         delivery systems.
AUTHOR(S):
                         Leigh, David A.; van Meurs, Sandra; Slater, Martin J.;
                         Murphy, Aden
CORPORATE SOURCE:
                         Centre for Supramolecular and Macromolecular
                         Chemistry, University of Warwick, Coventry, CV4 7AL,
```

Book of Abstracts, 219th ACS National Meeting, San

Francisco, CA, March 26-30, 2000 (2000), MEDI-008. American Chemical Society: Washington, D. C. CODEN: 69CLAC

SOURCE:

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

The discovery of a simple hydrogen bonding template for rotaxane formation has led to investigations into the potential of using

rotaxanes of biol. active peptides as novel drug

delivery systems. Here we describe how rotaxane formation imparts enzyme stability upon the peptide and how manipulation of the solubility and transport

properties can be achieved through functionalisation of the rotaxane macrocycle.

L13 ANSWER 9 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:653460 CAPLUS

DOCUMENT NUMBER: 132:141754

TITLE: Biodegradable polyrotaxanes as a drug carrier

AUTHOR(S): Ooya, T.; Yui, N.

CORPORATE SOURCE: School of Materials Science, Japan Advanced Institute of Science and Technology, Ishikawa, 923-1292, Japan

SOURCE: S.T.P. Pharma Sciences (1999), 9(1), 129-138 CODEN: STSSE5; ISSN: 1157-1489

PUBLISHER: Editions de Sante

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

A review with 51 refs. This article reviews our concept of drug delivery systems using drug/polyrotaxane conjugates as drug carriers. The biodegradable polyrotaxanes exhibit their supramol. architectures: many

\alpha-cyclodextrins are threaded onto a single poly(ethylene glycol) chain capped with biodegradable bulky end-groups. The synthetic method of the polyrotaxanes, the conjugation with drugs, and their association nature in a physiol. condition are described. The supramol. dissociation of the drug/polyrotaxane conjugates via terminal peptide cleavage by a hydrolytic

enzyme is discussed in relation to their association nature. Through these studies, advantages of drug/polyrotaxane conjugates as drug carriers are suggested in comparison with conventional drug/polymer conjugates.

REFERENCE COUNT: THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS 51 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 10 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:539755 CAPLUS

TITLE: Peptido[2]rotaxanes with oligosaccharide stoppers: A model system for controlled peptide

drug delivery.

AUTHOR(S): Leigh, David A.; Nepogodiev, Sergey A.

CORPORATE SOURCE: Department of Chemistry, University of Warwick,

Coventry, CV4 7AL, UK

SOURCE: Book of Abstracts, 218th ACS National Meeting, New

Orleans, Aug. 22-26 (1999), CARB-022. American Chemical Society: Washington, D. C.

CODEN: 67ZJA5

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

For efficient application as drugs, potent oligopeptides must overcome a number of phys. and enzymic barriers presented. Amongst these are the susceptibility of peptides to the action of hydrolytic enzymes and their poor membrane transport properties. Temporary encapsulation of peptides by a macrocycle in the form of [2]rotaxanes is proposed as a possible solution to these problems. For application as a drug delivery systems one of the stoppers attached to the end of oligopeptide thread should be degradable under physiol. conditions allowing the 'slippage' of the macrocycle. We investigated the application of oligosaccharides as biodegradable stoppers for [2]rotaxanes based on GlyGly. [2]Rotaxanes 1 and 2a were prepared through the 'clipping' strategy. After deprotection of the sugar portions of these compds. only rotaxane 2b was stable. The

disassembling of 2b can be achieved through the action of a-mannosidases.

L13 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:453602 CAPLUS

DOCUMENT NUMBER: 132:69125

TITLE: Polyrotaxanes: synthesis, structure, and potential in

drug delivery

Ooya, Tooru; Yui, Nobuhiko

School of Materials Science, Japan Advanced Institute CORPORATE SOURCE: of Science and Technology, Ishikawa, 923-1292, Japan CODEN: CRTSEO; ISSN: 0743-4863

SOURCE: Critical Reviews in Therapeutic Drug Carrier Systems (1999), 16(3), 289-330

PUBLISHER:

Begell House, Inc. DOCUMENT TYPE: Journal; General Review

LANGUAGE:

SOURCE:

English

This article reviews with 91 refs. the potential of polyrotaxanes in drug delivery with the historical background of polyrotaxane syntheses. Pseudopolyrotaxanes and polyrotaxanes, including classifications, synthetic methods, structures and phys. properties are discussed in the first section. The second section provides our concept of drug carriers using drug-polyrotaxane conjugates in comparison with conventional drug-polymer conjugates. The third and fourth sections describe the synthetic method for biodegradable polyrotaxanes, the conjugation with drugs, and their association under physiol. conditions. The fifth section discusses other possibilities for the polyrotaxanes such as drug penetration enhancers. These studies suggest the potential of polyrotaxanes in pharmaceutical applications.

REFERENCE COUNT: 91 THERE ARE 91 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 12 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:206406 CAPLUS

DOCUMENT NUMBER: 131:78242

TITLE: Synthesis of theophylline-polyrotaxane conjugates and their drug release via supramolecular dissociation

AUTHOR(S):

Ooya, Tooru; Yui, Nobuhiko CORPORATE SOURCE: School of Materials Science, Japan Advanced Institute

of Science and Technology, Tatsunokuchi, Ishikawa,

923-1292, Japan

Journal of Controlled Release (1999), 58(3),

251-269

CODEN: JCREEC: ISSN: 0168-3659

PUBLISHER: Elsevier Science Ireland Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Theophylline-polyrotaxane conjugates were synthesized by coupling theophylline with α -cyclodextrins (α -CDs) in the polyrotaxane. The polyrotaxane is a mol. assembly in which many α-CDs are threaded onto a poly(ethylene glycol) (PEG) chain capped with L-phenylalanine (L-Phe). Theophylline-7-acetic acid was activated by coupling with 4-nitrophenol, and then ethylenediamine was allowed to react with the active ester in order to obtain N-aminoethyltheophylline-7-acetoamide. This derivative was coupled with a 4-nitrophenyl chloroformate-activated polyrotaxane to obtain the theophylline-polyrotaxane conjugates. The conjugates formed a specific association under physiol. conditions, depending upon interactions between the theophylline mols. and/or the terminal L-Phe moiety in the conjugates. In vitro degradation of the conjugates revealed that theophylline-immobilized α -CDs were completely released by hydrolysis of the terminal peptide linkage in the polyrotaxane. This result indicates that the association of the conjugates does not induce the

steric hindrance but rather enhances the accessibility of enzymes to the

terminal peptide linkages. It is suggested that our designed drug-polyrotaxane conjugates can release the drugs via the dissociation of the

supramol. structure without steric hindrance of enzymic accessibility to

the terminal peptide linkages.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:482084 CAPLUS

DOCUMENT NUMBER: 129:265277

TITLE: New approach to drug targeting using a

drug-polyrotaxane conjugate AUTHOR(S): Ooya, Tooru; Yui, Nobuhiko

CORPORATE SOURCE: Japan Advanced Institute of Science and Technology,

Ishikawa, 923-1292, Japan

SOURCE: Proceedings of the International Symposium on

Controlled Release of Bioactive Materials (1998), 25th, 860-861

CODEN: PCRMEY; ISSN: 1022-0178

PUBLISHER: Controlled Release Society, Inc.

DOCUMENT TYPE: Journal LANGUAGE: English

A novel supramol.-structured drug conjugate using a polyrotaxane was prepared In vitro degradation of the conjugate revealed that

theophylline-modified a-cyclodextrin were released by terminal

hydrolysis of the polyrotaxane. The drug release via supramol. dissoln.

can feasibly be used for dual drug targeting.

REFERENCE COUNT: THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS 4 RECORD, ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 14 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:406136 CAPLUS

DOCUMENT NUMBER: 129:78839

TITLE: Method for the formation of non-aggregating

fluorescent conjugates by producing stable rotaxane-like inclusion complexes to be used in UV spectroscopy, fluorescence microscopy and flow

cytometry

INVENTOR(S): Aspe, Daniel

PATENT ASSIGNEE(S): Cis Bio International, Fr.; Aspe, Daniel

SOURCE: PCT Int. Appl., 37 pp.

CODEN: PIXXD2 DOCUMENT TYPE: Patent

LANGUAGE: French FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PAT	TENT	NO.			KIN	D	DATE			APPL:	ICAT	ION	NO.		D	ATE	
WO	9826	287			A1	_	1998	0618		WO 1:	997-	FR22	88		1	9971:	212 <
	W:	AL,	AM,	AT,	AU,	AZ,	BA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CU,	CZ,	DE,
		DK,	EE,	ES,	FI,	GB,	GE,	GH,	GM,	GW,	HU,	ID,	IL,	IS,	JP,	KΕ,	KG,
		KP,	KR,	ΚZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MD,	MG,	MK,	MN,	MW,	MX,
		NO,	NZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ΤJ,	TM,	TR,	TT,
		UA,	UG,	US,	UZ,	VN,	YU,	zw									
	RW:	GH,	GM,	KE,	LS,	MW,	SD,	SZ,	UG,	ZW,	ΑT,	BE,	CH,	DE,	DK,	ES,	FI,
		FR,	GB,	GR,	IE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	ΒJ,	CF,	CG,	CI,	CM,
		GA,	GN,	ML,	MR,	NE,	SN,	TD,	TG								
FR	2757	162			A1		1998	0619		FR 1	996-	1526	1		1:	9961:	212 <
FR	2757	162			В1		1999	0326									
CA	2272	890			A1		1998	0618		CA 1	997-	2272	890		1	9971:	212 <
CA	2272	890			C		2004	1130									

EP	9854894 946870		A A1	19980703 19991006	AU 1998-54894 EP 1997-951325		9971212 < 9971212 <
EP	946870		B1	20021127			
	R: AT,	BE, CH,	DE,	DK, ES, FR,	GB, GR, IT, LI, LU,	NL, SE,	MC, PT,
	IE,	FI					
JP	20015060	02	T	20010508	JP 1998-526322	1	9971212 <
JP	3955638		B2	20070808			
AT	228656		T	20021215	AT 1997-951325	1	9971212 <
ES	2187834		Т3	20030616	ES 1997-951325	1	9971212 <
US	6120987		A	20000919	US 1998-95471	1	9980610 <
PRIORIT	APPLN.	INFO.:			FR 1996-15261	A 1	9961212
					WO 1997-FR2288	W 1	9971212

AB The invention concerns a method for obtaining a fluorescent conjugate between a binding mol. having at least an amino, hydroxy, carboxy and/or sulfydryl group and a fluorophore reagent having at least a functional group capable of reacting with said amino, hydroxy, carboxy and/or sulfydryl group(s), in the presence of an aqueous solution of a water-soluble macrocycle. The binding mol. conjugates to the fluorophore and in the presence of the macrocycle a stable rotaxane-like inclusion complex is formed; thus the aggregation of the fluorescent conjugates is prevented. The macrocycle is a cyclodextrin, a cyclodextrin derivative, or a calixarene. Reactive fluorophores are e.g. cyanine dyes, fluorescein etc. The binding mols. can be antibodies, antigens, proteins, avidin, haptens, toxins, hormones , drugs, polymers, glass, polysaccharides, nucleic acids etc. The invention also concerns the conjugates obtained by this method and

their use. REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS

L13 ANSWER 15 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN

1997:339997 CAPLUS ACCESSION NUMBER:

127:70694 DOCUMENT NUMBER:

TITLE: Synthesis and characterization of biodegradable

polyrotaxane as a novel supramolecular-structured drug

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

carrier

AUTHOR(S): Ooya, Tooru; Yui, Nobuhiko

CORPORATE SOURCE: School of Materials Science, Japan Advanced Institute

of Science and Technology, Tatsunokuchi, Ishikawa,

923-12, Japan Journal of Biomaterials Science, Polymer Edition (

1997), 8(6), 437-455

CODEN: JBSEEA: ISSN: 0920-5063

VSP

DOCUMENT TYPE: Journal LANGUAGE:

SOURCE:

PUBLISHER:

English AB Polyrotaxanes were synthesized as novel biodegradable polymers with supramol, assembly and their properties evaluated in vitro. The synthesis of biodegradable polyrotaxanes consists of three steps: preparation of an inclusion complex consisting of α -cyclodextrins (α -CDs) and amino-terminated poly(ethylene glycol) (PEG); introduction of L-phenylalanine (L-Phe) at each complex terminal via peptide linkages; and hydroxypropylation of α -CDs in the polyrotaxanes. Succinimide ester of benzyloxycarbonyl-L-Phe was condensed with the terminal amino groups of the inclusion complex. 1H-NMR and GPC results showed that $\alpha\text{-CDs}$ were threaded onto a PEG chain and L-Phe moieties were introduced at each terminal of the PEG chain. Further, the amount of threaded α -CDs was found to be governed by the mol. weight of PEG. The hydroxypropylation of lpha-CDs improved the solubility of the polyrotaxanes in PBS (pH 7.4). The hydroxypropylated (HP-) polyrotaxanes were characterized by terminal peptide cleavage using papain. In vitro degradation of HP-polyrotaxanes revealed that $HP-\alpha$ -CDs threaded onto a PEG chain were released only when terminal peptide linkages were cleaved. Moreover, threaded

 $HP-\alpha$ -CDs chain were released only when terminal peptide linkages were cleaved. Moreover, threaded HP-α-CDs onto a PEG chain was found to be completely released. Kinetics of terminal peptide cleavage were also evaluated by catalytic efficiency (kcat/Km). The kcat/Km values were found to be independent of the mol. weight of HP-polyrotaxanes but to be affected by terminal hydrophobic moieties. It is proposed that our designed polyrotaxanes are feasible as novel drug carriers.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 16 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1996:489035 CAPLUS

DOCUMENT NUMBER: 125:177188

TITLE: Novel design of supramolecular-structured biodegradable polymer for drug delivery

AUTHOR(S): Yui, Nobuhiko; Ooya, Tooru

CORPORATE SOURCE: Sch. Materials Science, JAIST, Ishikawa, 923-12, Japan

SOURCE: Advanced Biomaterials in Biomedical Engineering and Drug Delivery Systems, [Iketani Conference on Biomedical Polymers], 5th, Kagoshima, Japan, Apr.

18-22, 1995 (1996), Meeting Date 1995,

333-334. Editor(s): Ogata, Naova. Springer: Tokvo,

Japan. CODEN: 63CXA6 Conference

DOCUMENT TYPE: LANGUAGE:

English Biodegradable polymers with supramol. structures were proposed as a novel candidate of substrates for temporal drug delivery. A biodegradable

polyrotaxane was synthesized in which α -cyclodextrins (α -CDs) as drug carriers were threaded onto a poly(ethylene glycol) (PEG) chain capped at each terminal with L-phenylalanine (L-Phe) via peptide linkages. The release of a-CDs from the biodegradable polyrotaxane was observed only when the terminal peptide linkages were hydrolyzed by papain. Further, the dethreading process of α -CDs from PEG chains was also observed to be quite rapid. Therefore, it is suggested that $\alpha\text{-CD}$ release from the biodegradable polyrotaxane was controlled by the hydrolysis of terminal peptide linkages.

L13 ANSWER 17 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1996:377201 CAPLUS

DOCUMENT NUMBER: 125:41804

TITLE: Biodegradable medicinal polymer assembly with

supermolecular structure

INVENTOR(S): Yui, Nobuhiko PATENT ASSIGNEE(S): Japan

SOURCE: PCT Int. Appl., 15 pp. CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA'	TENT				KIN		DATE			APPL		ION			D.	ATE	
WO	9609	073			A1		1996	0328		WO 1	995-	JP90	9		1	9950	512 <
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		ΤJ,	TM,	TT,	UA,	UG,	US,	UZ,	VN								
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		LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	ML,	MR,	NE,
		SN,	TD,	TG													
JP	0809	2130			A		1996	0409		JP 1	994-	2548	72		1	9940	924 <

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JP 3699141
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                                                         19950512 <--
    AU 9524199
                     A
                           19960409 AU 1995-24199
                                                         19950512 <--
    EP 730869
                     A1
                          19960911 EP 1995-918178
                                                         19950512 <--
    EP 730869
                     B1
                          20010627
       R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
    CN 1135720 A 19961113 CN 1995-190936
                                                        19950512 <--
                                     AT 1995-918178
    AT 202486
                     T
                          20010715
                                                         19950512 <--
    US 5855900
                                     US 1996-637733
                                                         19960426 <--
                     A
                          19990105
                                     JP 1994-254872
PRIORITY APPLN. INFO.:
                                                      A 19940924
                                     WO 1995-JP909
                                                       W 19950512
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The invention relates to a highly water-soluble polymer having arbitrarily controllable drug-carrying capacity and drug-releasing characteristics and serving as a novel drug carrier widely applicable in vivo; and a biodegradable medicinal polymer assembly having a supermol. structure and being capable of releasing a drug in response to a specific biodegrdn. occurring in each disease. The assembly comprises a number of drug-carrying cyclic compds. prepared by binding a drug to α , β or y-cyclodextrin, a linear polymer penetrating through the hollows of the cyclic compds., and biodegradable moieties bonded to both ends of the polymer. A biodegradable medicinal polymer assembly with supermol. structure for mitomycin C delivery is given as an example.

L13 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1996:267862 CAPLUS

DOCUMENT NUMBER: 125:41536

TITLE: Biodegradable polyrotaxanes for drug delivery

Yui, Nobuhiko AUTHOR(S):

CORPORATE SOURCE: Grad, Sch., Hokuniku Univ., Japan Kobunshi (1996), 45(4), 263 SOURCE:

CODEN: KOBUA3; ISSN: 0454-1138 PUBLISHER: Kobunshi Gakkai

DOCUMENT TYPE: Journal; General Review

LANGUAGE: Japanese

AB A review with 5 refs. discussing biodegradable polyrotaxanes for use in drug delivery systems.

L13 ANSWER 19 OF 20 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on

STN

ACCESSION NUMBER: 2000:222509 BIOSIS

DOCUMENT NUMBER: PREV200000222509

Peptide rotaxanes as potential drug TITLE:

delivery systems.

Leigh, David A. [Reprint author]; van Meurs, Sandra AUTHOR(S):

[Reprint author]; Slater, Martin J.; Murphy, Aden [Reprint

author]

CORPORATE SOURCE: Centre for Supramolecular and Macromolecular Chemistry,

Department of Chemistry, University of Warwick, Gibbet Hill

Road, Coventry, CV4 7AL, UK

Abstracts of Papers American Chemical Society, (SOURCE:

2000) Vol. 219, No. 1-2, pp. MEDI 8. print.

Meeting Info.: 219th Meeting of the American Chemical

Society. San Francisco, California, USA. March 26-30, 2000.

American Chemical Society. CODEN: ACSRAL. ISSN: 0065-7727.

DOCUMENT TYPE: Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 31 May 2000

Last Updated on STN: 5 Jan 2002

L13 ANSWER 20 OF 20 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on

ST

ACCESSION NUMBER: 1999:412609 BIOSIS

DOCUMENT NUMBER: PREV199900412609

TITLE: Peptido(2)rotaxanes with oligosaccharide stoppers: A model system for controlled peptide

drug delivery.

AUTHOR(S): Leigh, David A. [Reprint author]; Nepogodiev, Sergey A.

[Reprint author]

CORPORATE SOURCE: Department of Chemistry, University of Warwick, Coventry,

CV4 7AL, UK

SOURCE: Abstracts of Papers American Chemical Society, (

1999) Vol. 218, No. 1-2, pp. CARB 22. print.

Meeting Info.: 218th National Meeting of the American Chemical Society, Parts 1 and 2. New Orleans, Louisiana,

USA. August 22-26, 1999. American Chemical Society. CODEN: ACSRAL. ISSN: 0065-7727.

DOCUMENT TYPE: Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)
LANGUAGE: English

ENTRY DATE: Entered STN: 8 Oct 1999

Last Updated on STN: 8 Oct 1999

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